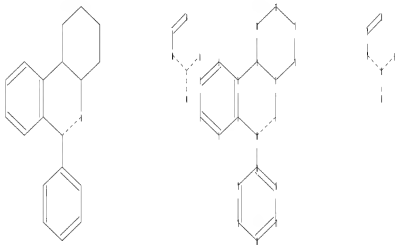


Print selected from 10589082.trn

=>
Uploading C:\Program Files\Stnexp\Queries\10589082.str



```
chain nodes :
21 22 24
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20
ring/chain nodes :
23 25 26
chain bonds :
10-15 21-22 21-23 22-24 24-25 24-26
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13
13-14 15-16 15-20 16-17 17-18 18-19 19-20
exact/norm bonds :
5-7 6-10 7-8 7-11 8-9 8-14 9-10 11-12 12-13 13-14 21-22 21-23 22-24
24-25 24-26
exact bonds :
10-15
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 15-16 15-20 16-17 17-18 18-19 19-20
```

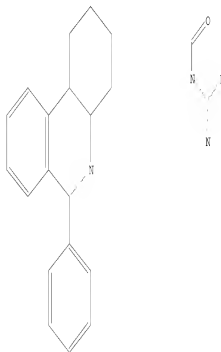
```
MATCH level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:Atom 21:CLASS
22:CLASS 23:CLASS 24:CLASS 25:CLASS 26:CLASS
```

L1 STRUCTURE UPLOADED

=> d l1

Print selected from 10589082.trn

L1 HAS NO ANSWERS
L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> s l1
SAMPLE SEARCH INITIATED 18:29:20 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 9 TO ITERATE

100.0% PROCESSED 9 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 9 TO 360
PROJECTED ANSWERS: 2 TO 124
```

L2 2 SEA SSS SAM L1

```
=> d scan
SCAN IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=) .
```

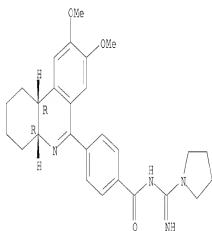
=> d scan

```
L2 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-
```

Print selected from 10589082.trn

phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)-
MF C27 H32 N4 O3

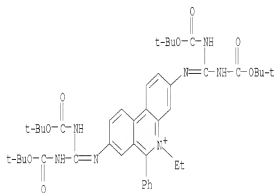
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

L2 2 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3,8-bis[[(1,1-dimethylethoxy)carbonyl]amino]methyl-
ne]amino]-5-ethyl-6-phenyl-
MF C43 H56 N7 O8
CI COM



ALL ANSWERS HAVE BEEN SCANNED

=> d his

Page 3

Print selected from 10589082.trn

(FILE 'HOME' ENTERED AT 18:28:42 ON 03 MAR 2008)

FILE 'REGISTRY' ENTERED AT 18:29:00 ON 03 MAR 2008
L1 STRUCTURE UPLOADED
L2 2 S L1

=> s l1 full
FULL SEARCH INITIATED 18:29:51 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 167 TO ITERATE

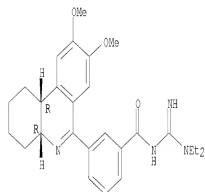
100.0% PROCESSED 167 ITERATIONS 25 ANSWERS
SEARCH TIME: 00.00.01

L3 25 SEA SSS FUL L1

=> d scan

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-3-[(4aR,10bR)-1,2,3,4,4a,10b-
hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C27 H34 N4 O3

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

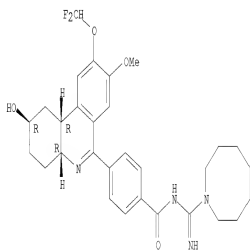
HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):2000

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, 4-[(12a,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-
hydroxy-8-methoxy-6-phenanthridinyl]-N-[(hexahydro-1(2H)-
azepinyl)iminomethyl]-, rel-
MF C30 H36 F2 N4 O4

Relative stereochemistry.

Page 4

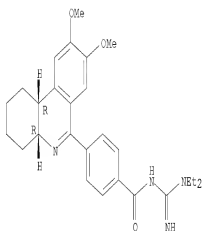
Print selected from 10589082.trn



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(3,5-dimethyl-1H-pyrazol-1-yl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C27 H34 N5 O3

Absolute stereochemistry.

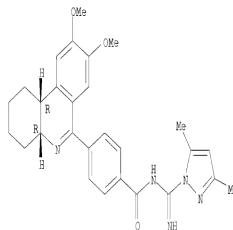


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Print selected from 10589082.trn

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(3,5-dimethyl-1H-pyrazol-1-yl)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C28 H31 N5 O3

Absolute stereochemistry.

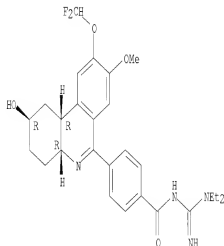


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel-
MF C27 H32 F2 N4 O4

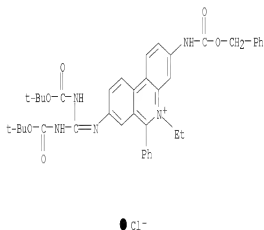
Relative stereochemistry.

Print selected from 10589082.trn



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

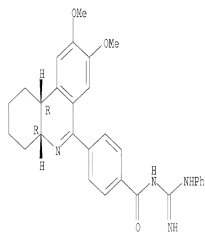
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN
IN Phenanthridinium, 8-[[bis[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[[phenylmethoxy]carbonyl]amino]-, chloride (9CI)
MF C40 H44 N5 O6 . Cl



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN
IN Benzamide, 4-[[[4aR,10bR]-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(phenylamino)methyl]-
MF C29 H30 N4 O5

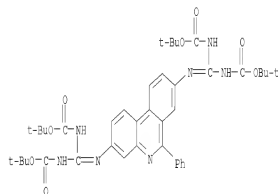
Absolute stereochemistry.

Print selected from 10589082.trn



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN
IN Carbamic acid, [[(6-phenyl-3,8-phenanthridinediyl)bis(nitrilomethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI)
MF C41 H51 N7 O8

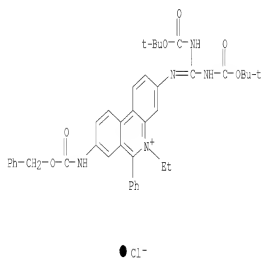


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN
IN Phenanthridinium, 3-[[bis[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[[phenylmethoxy]carbonyl]amino]-, chloride (9CI)

Print selected from 10589082.trn

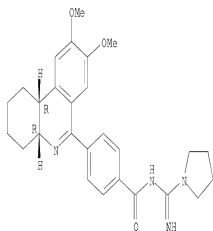
MF C40 H44 N5 O6 . Cl



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN

IN Benzanide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)-
 MF C27 H32 N4 O3

Absolute stereochemistry.

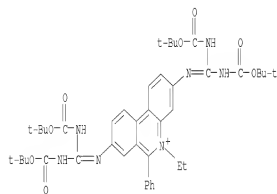


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Print selected from 10589082.trn

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN

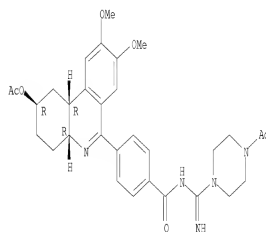
IN Phenanthridinium, 3,8-bis[[bis[(1,1-dimethylethoxy)carbonyl]amino]methyl
 ne]amino]-5-ethyl-6-phenyl-
 MF C43 H56 N7 O8
 Cl COM



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on SIN

IN Benzanide, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[(4-acetyl-1-piperazinyl)iminomethyl]-,
 rel-
 MF C31 H37 N5 O6

Relative stereochemistry.

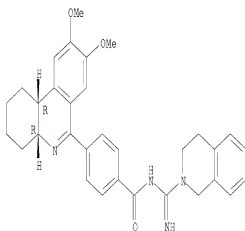


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Print selected from 10589082.trn

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(3,4-dihydro-2(1H)-isoquinolinyl)iminomethyl]-4-[(4aR,10bR)-
1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C32 H34 N4 O3

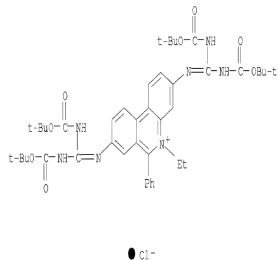
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

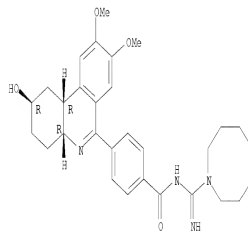
L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 3,8-bis[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-, chloride (9CI)
MF C43 H56 N7 O8 . Cl

Print selected from 10589082.trn



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-4-[(2R,4aR,10bR)-
1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel-
MF C30 H38 N4 O4

Relative stereochemistry.

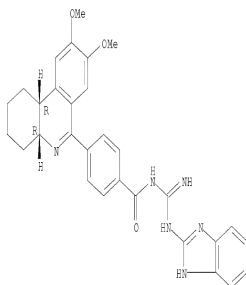


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzamide, N-[amino(18-benzimidazol-2-ylamino)methylene]-4-[(4aR,10bR)-
1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (9CI)
MF C30 H38 N6 O3

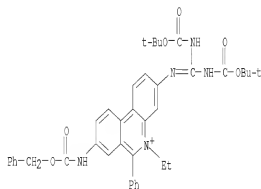
Print selected from 10589082.trn

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STM
IN Phenanthridinium, 3-[[bis[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-9-[[[phenylmethoxy]carbonyl]amino]-
MF C40 H44 N5 O6
CI COM

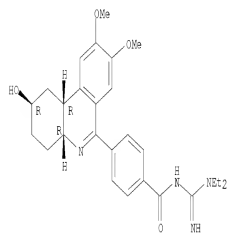


L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STM
IN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-3,9-dimethoxy-6-phenanthridinyl]-, rel-

Print selected from 10589082.trn

MF C27 H34 N4 O4

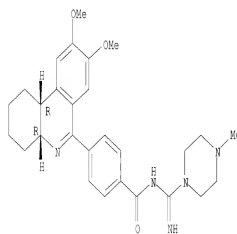
Relative stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STM
IN Benzamide, 4-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(4-methyl-1-piperazinyl)methyl]-
MF C28 H35 N5 O3

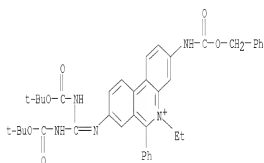
Absolute stereochemistry.



Print selected from 10589082.trn

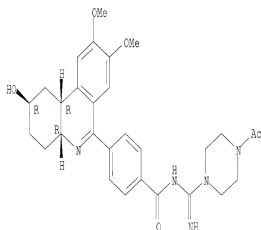
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Phenanthridinium, 8-[[bis[[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[[phenylmethoxy]carbonyl]amino]-
C40 H44 NS O6
CF CUM



L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzanide, N-[[[4-acetyl-1-piperazinyl]iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel-
C29 H35 NS O5

Relative stereochemistry.

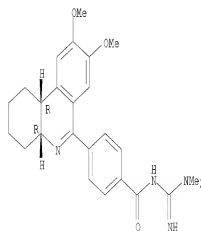


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

Print selected from 10589082.trn

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzanide, N-[[[dimethylamino]iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-
MF C25 H30 N4 O3

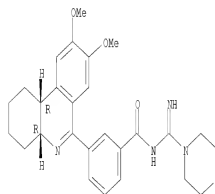
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzanide, 3-[[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinyl)methyl]-
MF C27 H32 N4 O4

Absolute stereochemistry.

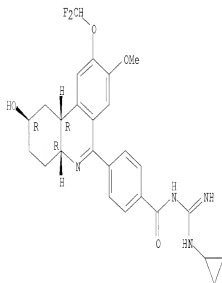


Print selected from 10589082.ttn

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzanide, N-[(cyclopropylamine)iminomethyl]-4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-phenanthridinyl]-, rel-
MF C28 H28 F2 N4 O4

Relative stereochemistry.

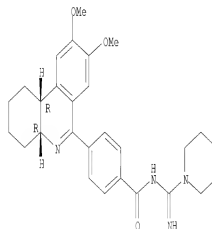


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L3 25 ANSWERS REGISTRY COPYRIGHT 2008 ACS on STN
IN Benzanide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)-
MF C27 H32 N4 O4

Absolute stereochemistry.

Print selected from 10589082.ttn



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=> file caplus
FILE 'CAPLUS' ENTERED AT 18:30:14 ON 03 MAR 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

Copyright of the articles to which records in this database refer is held by the publishers listed in the PUBLISHER (PB) field (available for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications. The CA Lexicon is the copyrighted intellectual property of the American Chemical Society and is provided to assist you in searching databases on STN. Any dissemination, distribution, copying, or storing of this information, without the prior written consent of CAS, is strictly prohibited.

FILE COVERS 1907 - 3 Mar 2008 VOL 148 ISS 10
FILE LAST UPDATED: 2 Mar 2008 (20080302/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

<http://www.cas.org/infopolicy.html>

=> s 13
14 5 13

=> d cblb abs hitstr 1-5

14 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

2005:902858 Document No. 143:248297 Preparation of guanidiny
hydroxyphenylphenanthridines as PDE4 inhibitors. Schmidt, Beate;
Flockert, Dieter; Hatzelmann, Armin; Zitt, Christof; Barsig, Johannes;
Marx, Dejenhard; Kley, Hans-Peter; Kautz, Ulrich (Altana Pharma A.-G.,
Germany). POT Int. Appl. WO 2005/7906 A1 20050825, 72 pp. DESIGNATED
STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BW, BY, BT, CA,
CH, CN, CO, CR, CU, CZ, DE, DK, DR, DZ, EC, EE, EG, ES, FI, GE, GR, GD,
GH, GM, GN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NZ, NA, NI, NO, NU, PG, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TR, TT, UA, UG,
US, VE, VC, VN, YU, ZA, ZM, ZW; R: AT, BE, BF, BG, CF, CG, CH, CI,
CM, CN, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, MD, NE, NG,
NL, PT, SE, SN, SD, TG, TR. (English). CODES: PIXDD2. APPLICATION: WO
2004-3592 20040219. PRIORITY: EP 2004-3592 20040219.

GT

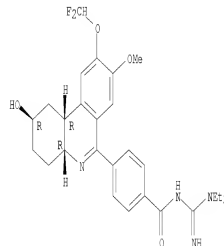
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = OH, alkoxy, cycloalkoxy, etc.; R2 = OH,
cycloalkylmethoxy, cycloalkoxy, etc. or R1 and R2 together form
alkylenedioxy group; R3 = H or alkyl; R4 = OR3 and R5 = H or alkyl or R4 =
H or alkyl and R5 = OR3; R6 = H or alkyl; R7 = (un)substituted guanidiny;
R8 = H, halo, nitro, etc.; R9 = H, alkyl, alkoxyalkyl, etc.] and their
pharmaceutically acceptable salts, are prepared and disclosed as
phosphodiesterase 4 (PDE4) inhibitors. Thus, e.g., II was prepared by
coupling of 4-((2R,4aR,10bR)-2-acetoxy-8,9-dimethoxy-1,2,3,4,4a,10b-
hexahydro-phenanthridin-6-yl)-benzoic acid with the resp. guanidiny
derivative followed by hydrolysis. The activity of I was evaluated using
scintillation proximity assays and it was revealed that selected compds.
of the invention displayed -log IC50 values higher than 7.5. I as
inhibitor of PDE4 should provide useful in the treatment of respiratory
disorders. Pharmaceutical compns. comprising I are disclosed.

II 862993-72-4P 862993-73-5P 862993-74-6P
862993-75-7P 862993-76-8P 862993-77-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(preparation of guanidiny hydroxyphenylphenanthridines as PDE4 inhibitors)

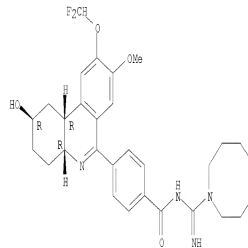
RN 862993-72-4 CAPLUS
CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-
(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-
phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



RN 862993-73-5 CAPLUS
CN Benzamide, 4-[(2R,4aR,10bR)-9-(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-
hydroxy-8-methoxy-6-phenanthridinyl]-N-[(hexahydro-1(2H)-
azocinyl)iminomethyl]-, rel- (CA INDEX NAME)

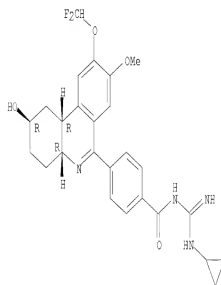
Relative stereochemistry.



RN 862993-74-6 CAPLUS
CN Benzamide, N-[(cyclopropylamino)iminomethyl]-4-[(2R,4aR,10bR)-9-
(difluoromethoxy)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8-methoxy-6-
phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.

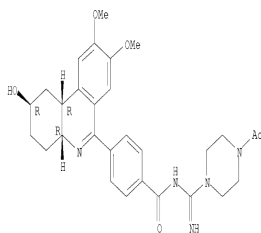
Print selected from 10589082.trn



RN 862993-75-7 CAPLUS

CN Benzamide, N-[(4-acetyl-1-piperazinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.

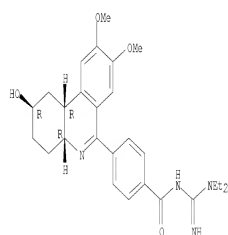


RN 862993-76-8 CAPLUS

CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.

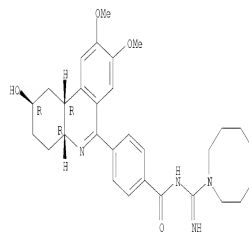
Print selected from 10589082.trn



RN 862993-77-9 CAPLUS

CN Benzamide, N-[(hexahydro-1(2H)-azocinyl)iminomethyl]-4-[(2R,4aR,10bR)-1,2,3,4,4a,10b-hexahydro-2-hydroxy-8,9-dimethoxy-6-phenanthridinyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



IT 862993-78-0P

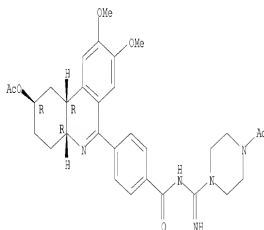
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(preparation of guanidyl hydroxyphenylphenanthridines as F0B4 inhibitors)

RN 862993-78-0 CAPLUS

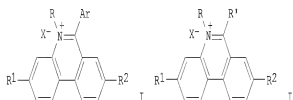
CN Benzamide, 4-[(2R,4aR,10bR)-2-(acetyloxy)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[(4-acetyl-1-piperazinyl)iminomethyl]-, rel- (CA INDEX NAME)

Relative stereochemistry.



14 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STM
 2005:158539 Document No. 142:261402 Preparation of phenanthridine
 derivatives as anti-viral agents. Tor, Yitzhak; Luedke, Nathan (The
 Regents of the University of California, USA). PCT Int. Appl. WO
 2005016343 A1 20050224, 58 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT,
 AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CY, DE, DK,
 DM, DG, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GR, HU, ID, IL, IN, IS,
 JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, ME, MK, MN,
 MW, MX, MY, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG,
 SK, SL, SY, TZ, TM, TN, TR, TT, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW;
 RW: AT, BE, BF, BJ, CF, CG, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB,
 GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TG, TO, TR. (English).
 CODEN: PIIKX2. APPLICATION: WO 2004-US26188 20040811. PRIORITY: US
 2003-49545P 20030811.

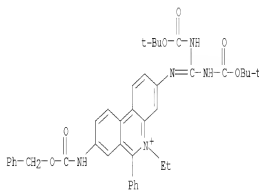
GI



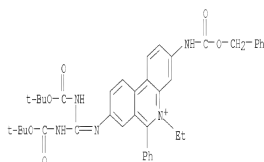
AB A series of substituted phenanthridine derivs. (e.g. ethidium derivs. I and II) (R, R' = each functionalized or unfunctionalized alkyl, alkenyl, alkynyl, aryl, aralkyl, heteroaryl, or alkylheteroaryl; wherein alkylheteroaryl refers to a straight-chain alkyl, alkenyl or alkynyl group where one of the hydrogen atoms bonded to a terminal carbon atom is replaced with a heteroaryl moiety; Ar = optionally substituted Ph or any aromatic residue; R1, R2 = independently selected from the group consisting of a urea, a substituted urea, a di-Boc-guanidino, conjugated amino acids, carbohydrates, NE2, 1-pyrrolyl, guanidino, and benzoyloxycarbonylamino) has been synthesized by converting the amines at the 3- and 8- positions of

ethidium bromide into guanidino, pyrrole, urea, and various substituted ureas. The resulting derivs. exhibit unique spectral properties that change upon binding nucleic acids. These compds. maximize the binding affinity of phenanthridine to viral RNA and DNA sites, while minimizing the binding to host cell DNA. The antiviral activity of the compds. can thus be maximized, while toxic and/or mutagenic side effects are minimized. The compds. have an enhanced affinity and specificity for HIV-1 rev response element as compared to ethidium bromide. Thus, ethidium bromide was acylated by Ph chloroformate in a mixture of 500 mM sodium phosphate buffer (pH 6.8) and acetone at room temperature for 10 min to give 3,8-bis(phenoxycarbonylamino)-6-phenyl-5-ethylphenanthridinium dihydrogenphosphate which was heated with NH3 in methanol in a pressure tube at 80° for 1 h to give 3,8-di(ureido)-6-phenyl-5-ethylphenanthridinium chloride (III). III in vitro showed the binding affinity to DNA with K_d of 106 nM, IC50 of >1/0 μ M μ g/ml against HIV-1 rev response element, IC50 of 15 μ M against HIV-1, and exhibited no toxicity against HeLa cells at 10 μ M.

IT 66(836-33-9D, 3-[N,N'-Bis(tert-butoxycarbonyl)guanidino]-8-(benzoyloxycarbonylamino)-6-phenyl-5-ethylphenanthridinium chloride 66(836-37-3D, 8-[N,N'-Bis(tert-butoxycarbonyl)guanidino]-3-(benzoyloxycarbonylamino)-6-phenyl-5-ethylphenanthridinium chloride 845858-38-0D, 3,8-Bis[N,N'-bis(tert-butoxycarbonyl)guanidino]-6-phenyl-5-ethylphenanthridinium chloride
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation of phenanthridine derivs. with selective viral nucleic acids-binding property as antiviral agents)
 RN 66(836-33-9 CAPLUS
 CN Phenanthridinium, 3-[[bis[[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)

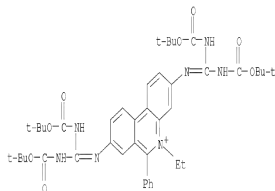


RN 66(836-37-3 CAPLUS
 CN Phenanthridinium, 8-[[bis[[[(1,1-dimethylethoxy)carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[[(phenylmethoxy)carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)

● Cl⁻

RN 845858-38-0 CAPLUS

CN Phenanthridinium, 3,8-bis[[(1,1-dimethylethoxy)carboxylamino]methyl]ne]amino]-5-ethyl-6-phenyl-, chloride (9CI) (CA INDEX NAME)

● Cl⁻

14 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS ON STN

2005:36679 Document No. 142:275617 Molecular Determinants for DNA Minor Groove Recognition: Design of a Bis-Guanidinium Derivative of Ethidium That Is Highly Selective for AT-Rich DNA Sequences. Bailly, Christian; Arzaf, Reem K.; Tanioue, Farid A.; Laine, William; Tard, Christelle; Lonsien, Amel; Colson, Pierre; Eykin, David W.; Wilson, W. David (INSERM U-504 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCU, Lille, 59045, Fr.). Biochemistry, 44(6), 1941-1952 (English) 2005. C.DEN: BICHM. ISSN: 0006-2360. OTHER SOURCES: CASREACT 142:275617. Publisher: American Chemical Society.

AB The phenanthridinium dye ethidium bromide is a prototypical DNA intercalating agent. For decades, this anti-trypanosomal agent has been known to intercalate into nucleic acids, with little preference for particular sequences. Only poly(dA)-poly(dT) tracts are relatively refractory to ethidium intercalation. In an effort to tune the sequence selectivity of known DNA binding agents, we report here the synthesis and detailed characterization of the mode of binding to DNA of a novel ethidium derivative possessing two guanidinium groups at positions 3 and 8. This compound, DB950, binds to DNA much more tightly than ethidium and exhibits distinct DNA-dependent absorption and fluorescence properties. The study of the mode of binding to DNA by means of circular and elec. linear dichroism revealed that, unlike ethidium, DB950 forms minor groove complexes with AT sequences. Accurate quantification of binding affinities by surface plasmon resonance using AuTr hairpin oligomers indicated that the interaction of DB950 is over 10-50 times stronger than that of ethidium and comparable to that of the known minor groove binder furazolidine. DB950 interacts weakly with GC sites by intercalation. DNase I footprinting expts. performed with different DNA fragments established that DB950 presents a pronounced selectivity for AT-rich sites, identical with that of furazolidine. The replacement of the amino groups of ethidium with guanidinium groups has resulted in a marked gain of both affinity and sequence selectivity. DB950 provides protection against DNase I cleavage at AT-containing sites which frequently correspond to regions of enhanced cleavage in the presence of ethidium. Although DB950 maintains a planar phenanthridinium chromophore, the compound no longer intercalates at AT sites. The guanidinium groups of DB950, just like the amidinium group of furazolidine (DB75), are the critical determinants for recognition of AT binding sites in DNA. The chemical modulation of the ethidium exocyclic amines is a profitable option to tune the nucleic acid recognition properties of phenylphenanthridinium dyes.

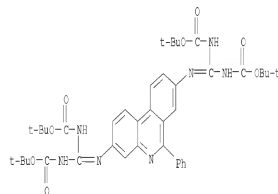
IT 847361-44-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(bis-guanidinium derivative of ethidium is highly selective for AT-rich DNA sequences)

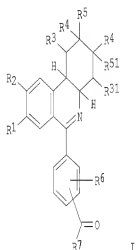
RN 847361-44-8 CAPLUS

CN Carbamic acid, [(6-phenyl-3,8-phenanthridinediyl)bis(nitrimethanetetrayl)]tetrakis-, tetrakis(1,1-dimethylethyl) ester (9CI) (CA INDEX NAME)



14 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS ON STN
 2004:182646 Document No. 140:235725 Preparation of 6-phenylphenanthridine derivatives as phosphodiesterase 4 (PDE4) inhibitors. Rley, Hans-Peter; Hatzelmann, Armin; Barsig, Johannes; Marx, Degenhard; Flockert, Dieter; Schmidt, Beate; Weinbrenner, Steffen (Altana Pharma A.-G., Germany). PCT Int. Appl. WO 2004/018431 A2 20040304, 49 pp. DESIGNATED STATES: W: AC, AL, AU, BA, BR, CA, CN, CO, DE, EC, EE, ES, FR, ID, IL, IN, IS, JP, KR, LI, LV, MA, ME, MX, NO, NZ, PH, PL, SG, TH, UA, US, VN, YU, ZA, ZW; SM: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, TR. (English). CODEN: PINKD2. APPLICATION: WO 2003-EP967 20030613. PRIORITY: EP 2002-18530 20020617.

GT



AB The title comds. [I; R1, R2 = H, C1-4 alkoxy, C3-7 cycloalkoxy, C3-7 cycloalkylmethoxy or completely or predominantly fluorine-substituted C1-4 alkoxy; or R1 and R2 together are a C1-2 alkylendioxy group; R3, R5 = H, C1-4 alkyl; or R3 and R5 together are a C1-4 alkylene group; R4 = H, C1-4 alkyl and R5 = H; or R5 and R5 together represent an addnl. bond; R6 = H, halogen, nitro, C1-4 alkyl, CF3, C1-4 alkoxy; R7 = (unsubstituted guanidino, heterocyclylamino, 1-heterocyclyl-1-(imino)methyl, etc.) or salts thereof, as well as N-oxides, enantiomers, E/Z isomers, or tautomers thereof and their salts are prepared. These comds. I are useful for producing pharmaceutical comds. for treating respiratory disorders and/or dermatoses. Also disclosed is a method for treating an illness treatable by administration of a PDE4 inhibitor in a patient comprising administering to said patient in need thereof a therapeutically effective amount of a compound of formula I, in particular airway disorders. W'-[1-[4-[(4aR,10bR)-6,9-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]phenyl]methanoyl]-N,N-diethylguanidine. Thus, 4.9 g 1,1-diethylguanidium sulfate was suspended in 120 mL MeCN, treated with 720 mg NaOH in 25 mL MeOH, and stirred at room temperature for 1 h. The solvent

was evaporated and the residue was suspended in 200 mL CH2Cl2, treated with 5.2 g Na2CO3 and then dropwise with a solution of 4.2 g 4-[(4aR,10bR)-6,9-

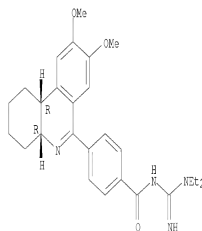
dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]benzoyl chloride hydrochloride in 200 mL CH2Cl2 dropwise, and stirred at room temperature for 15 h to give, after workup and silica gel chromatog., N'-[1-[4-[(4aR,10bR)-6,9-dimethoxy-1,2,3,4,4a,10b-hexahydrophenanthridin-6-yl]phenyl]methanoyl]-N,N-diethylguanidine (II). 12 Comds. I including II showed -logIC50 (mol/L) of >8 against phosphodiesterase 4.

IT 667422-55-1P 667422-57-3P 667422-58-4P
 667422-59-5P 667422-61-9P 667422-62-1P
 667422-63-1P 667422-64-2P 667422-65-3P
 667422-66-4P 667422-67-5P
 RU: PAC (Pharmacological activity); SPN (Synthetic preparation); THW (Therapeutic use); BIOL (Biological study); PREP (Preparation); USDS (Uses)
 [preparation of phenylphenanthridine derivs. as phosphodiesterase 4 (PDE4) inhibitors for treating respiratory disorders and/or dermatoses dermatosis]

RM 667422-55-1 CAPLUS

CN Benzamide, N-[(diethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.

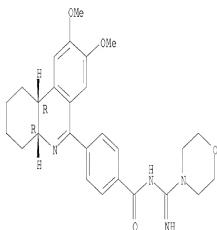


RM 667422-57-3 CAPLUS

CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

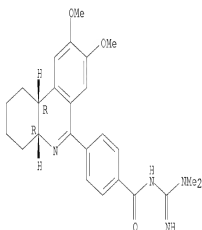
Print selected from 10589082.trn



RN 667422-58-4 CAPLUS

CN Benzamide, N-[(dimethylamino)iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.

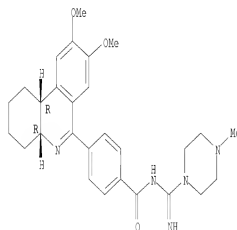


RN 667422-59-5 CAPLUS

CN Benzamide, 4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(4-methyl-1-piperazinyl)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

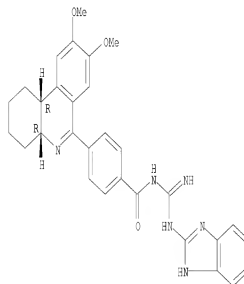
Print selected from 10589082.trn



RN 667422-61-9 CAPLUS

CN Benzamide, N-[amino(1H-benzimidazol-2-ylamino)methylene]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

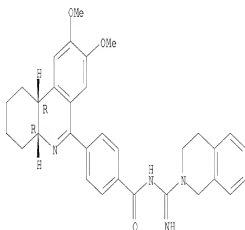


RN 667422-62-0 CAPLUS

CN Benzamide, N-[13,4-dihydro-2(1H)-isoquinolinyl]iminomethyl]-4-[(4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

Absolute stereochemistry.

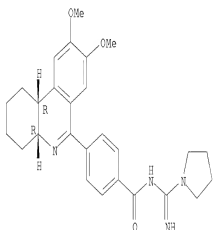
Print selected from 10589082.trn



RN 667422-63-1 CAPLUS

CN Benzamide, 4-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-1-pyrrolidinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.

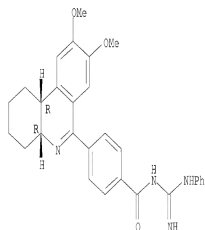


RN 667422-64-2 CAPLUS

CN Benzamide, 4-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-[imino(phenylamino)methyl]- (CA INDEX NAME)

Absolute stereochemistry.

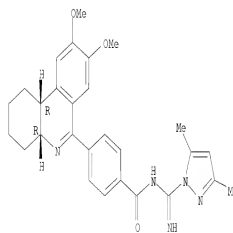
Print selected from 10589082.trn



RN 667422-65-3 CAPLUS

CN Benzamide, N-[(3,5-dimethyl-1H-pyrazol-1-yl)iminomethyl]-4-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

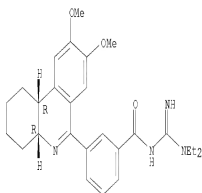
Absolute stereochemistry.



RN 667422-66-4 CAPLUS

CN Benzamide, N-[(diethylamino)iminomethyl]-3-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]- (CA INDEX NAME)

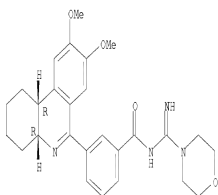
Absolute stereochemistry.



RN 667422-67-5 CAPLUS

CN Benzamide, 3-[[4aR,10bR)-1,2,3,4,4a,10b-hexahydro-8,9-dimethoxy-6-phenanthridinyl]-N-(imino-4-morpholinylmethyl)- (CA INDEX NAME)

Absolute stereochemistry.



14 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

2003:867286 Document No. 140:192208 Synthesis, photophysical properties, and nucleic acid binding of phenanthridinium derivatives based on ethidium. Luedtke, Nathan W.; Liu, Qi; Tor, Yitzhak (Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, CA, 92093-0358, USA). *Bioorganic & Medicinal Chemistry*, 11(23), 5235-5247 (English) 2003. CODEN: BMECEP. ISSN: 0968-0896. OTHER SOURCES: CASREACT 140:192208. Publisher: Elsevier Ltd..

AB In an attempt to decrease the DNA affinity (and hence the toxicity and mutagenicity) of ethidium bromide, a series of substituted phenanthridine derivs. has been synthesized by converting the amines at the 3- and 8-positions of ethidium bromide into guanidine, pyrrole, urea, and various substituted ureas. The resulting derivs. exhibit unique spectral properties that change upon binding nucleic acids. The compds. were analyzed for their ability to inhibit the HIV-1 Rev-Rev Response Element (RRE) interaction, as well as for their affinity to calf thymus DNA. One derivative (3,8-bis-urea-ethylamine-5-ethyl-6-phenylphenanthridinium

trifluoroacetate) has an enhanced affinity and specificity for HIV-1 RRE as compared to ethidium bromide. These results indicate that the nucleic acid affinity and specificity of an intercalating agent can be tuned by synthetic modification of its exocyclic amines.

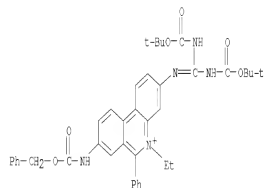
IT 660836-33-9P 660836-37-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PRGP (Preparation); RACT (Reactant or reagent)

(synthesis, photophys. properties, and nucleic acid binding of phenanthridinium derivs. based on ethidium)

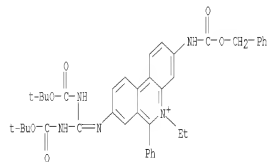
RN 660836-33-9 CAPLUS

CN Phenanthridinium, 3-[[bis[[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-8-[[[phenylmethoxy]carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)

● Cl⁻

RN 660836-37-3 CAPLUS

CN Phenanthridinium, 8-[[bis[[[1,1-dimethylethoxy]carbonyl]amino]methylene]amino]-5-ethyl-6-phenyl-3-[[[phenylmethoxy]carbonyl]amino]-, chloride (9CI) (CA INDEX NAME)

● Cl⁻

Print selected from 10589082.trn